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2020-07

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Kluger , N , Mähönen , K , Aitkoski , A , Hiltunen , E , Pankakoski , A , Panelius , J & Lappalainen , K 2020 , ' Bullous pemphigoid-associated chronic atrophic gastritis ' , Dermatologic therapy , vol. 33 , no. 4 , 13671 . <https://doi.org/10.1111/dth.13671>

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<http://hdl.handle.net/10138/331897>

<https://doi.org/10.1111/dth.13671>

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Dermatologic Therapy

*Letter to the Editor*

## Bullous pemphigoid associated chronic atrophic gastritis

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Running head: Bullous pemphigoid and chronic atrophic gastritis

Key-word : B12 deficiency, bullous pemphigoid, chronic atrophic gastritis, pernicious anemia,

Conflicts of interest: none declared

Funding sources: none declared

Figure: 0

Table: 0

Word count: 540

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/dth.13671

Accepted Article

Dear Editor,

Bullous pemphigoid (BP) can be associated with various co-morbidities such as neurological disorders, hypertension or diabetes (Pankakoski, 2018). Organ-specific or non-organ specific autoimmune comorbidities have been also reported (Ljubojevic, 2012). They may have implication during the management of the patient. We report the fortuitous discovery of autoimmune atrophic chronic gastritis during the management of BP by methotrexate. To date, atrophic gastritis/pernicious anemia has been reported on two previous occasion (Obasi, 1977; Callen, 1978).

An otherwise healthy 72-year-old man was diagnosed with typical BP that evolved for a month. He had generalized tense blisters with pseudo-urticarial and eczematous lesions, linear deposits of IgG and C3 along the basement membrane zone on direct immunofluorescence and elevated circulating BP180 antibodies (140 U/mL, N<9). Clobetasol proprionate ointment daily was initiated with oral methotrexate (MTX, 10 mg the first week and then 15 mg weekly) and oral folic acid supplementation 5 mg the following day. At initiation mean corpuscular volume (MCV) was slightly elevated (102 fl) with low erythrocytes count ( $3.93 \times 10^9$ , N>4.25) without anemia. White blood count, creatinine, glomerular filtration rate, albumin level and liver enzymes were within normal ranges. At one-month follow-up, patient had considerably improved without any new blisters. At four-month follow-up, BP was in remission. MCV had meanwhile increased progressively up to 107 fl. Serum folate was within normal range while serum B12 levels were undetectable (< 5 pmol/L, N>35). B12 deficiency was confirmed on a second sample. Parietal cell antibodies were positive 45 U/mL (N<7), while intrinsic factor antibodies negative 1.08 AU/mL (N>1.53). Patient was supplemented by oral cyanocobalamin 1 mg/day. After three months

of oral supplementation, MCV and erythrocyte count were within normal range. Biopsies of the corpus mucosa during gastroscopy confirmed chronic atrophic gastritis without ulcer or cancer. *Helicobacter pylori* was absent. The daily supplement of 1 mg cyanocobalamine was not associated with any loss of MTX efficacy against BP.

We report here a case of atrophic gastritis associated with BP. Chronic gastritis is quite frequent in Nordic countries (Sipponen, 2015). It is usually associated with *H. pylori* infection in 90% of the cases. The rest of the cases can be of auto-immune origin with auto-antibodies against parietal cells and/or intrinsic factor (Sipponen, 2015). To the best of our knowledge two previous patients, both women aged 74 and 70 years, were diagnosed with pernicious anemia (PA). In the first case, a 74-year-old woman had had PA from 29 years before BP onset. In the second case, it was a fortuitous finding at the time of BP diagnosis in a 70-year-old woman. The association of both conditions may be of course fortuitous or under-reported as chronic gastritis is a frequent finding. Mechanisms underlying a possible link include: cross-reactivity of autoantibodies between tissues, epitope spreading, or linkage to human leukocytes antigen alleles (Narla, 2020). In a national inpatient sample of US hospitalizations, Narla *et al.* found that BP was associated with an elevated number of autoimmune diseases, vitiligo and chronic urticaria especially (Narla, 2020). BP was also found to be associated with PA, but the association was not significant after adjustment in multivariable models.

As MTX is a common treatment in BP (Feliciani, 2015), this differential diagnosis should be kept in mind in case of unexplained increase of MCV during treatment of patients with BP.

Conflict of interest: none declared

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